

--22. A bifunctional fusion glycoprotein or conjugate thereof comprising:

- (i) at least one first portion which possesses enzymatic activity; and
- (ii) at least one second portion that binds said first component to a tumor-specific antigen on a tumor cell;

wherein said glycoprotein or conjugate thereof comprises at least one carbohydrate complement comprising at least one exposed carbohydrate residue selected from the group consisting of mannose, galactose, N-acetylglucosamine, N-acetyllactose, glucose and fucose.

23. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 22, wherein said exposed carbohydrate residue is a galactose or a mannose.

24. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 22, wherein said first portion consists essentially of an enzyme.

25. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 24, wherein said enzyme is selected from the group consisting of penicillin G amidase, penicillin V amidase,  $\beta$ -lactamase, alkaline phosphatase, carboxypeptidase G2, carboxypeptidase A, cytosine deaminase, nitroreductase, diaphorase, arylsulfatase, glycosidase,  $\beta$ -glucosidase, and  $\beta$ -glucuronidase.

26. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 22, wherein said first portion consists essentially of a catalytic antibody.

27. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 22, wherein said tumor specific antigen to which said second portions binds comprises a tumor associated antigen selected from the group consisting of CEA, N-CAM, N-cadherin, PEM, GICA, TAG-72, TF $\beta$ , GM3, GD3, GM2, GD2, GT3, HMWMAA, pMel17, gp113 (Muc18), p53, p97, MAGE-1, gp105, erbB2, EGF-R, PSA, transferrin-R, P-glycoprotein and cytokeratin.

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28. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 22, wherein said second portion consists essentially of an antibody or an antigen binding fragment thereof.

29. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 28, wherein said antibody or said antigen binding fragment thereof is a humanized antibody.

30. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 29, wherein said antibody is a monoclonal antibody or an antigen binding fragment thereof.

31. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 30, wherein said monoclonal antibody is the monoclonal antibody BW 431/26 or an antigen binding fragment thereof.

32. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 22, wherein said first portion and said second portion are connected by a linker molecule.

33. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 32 having the formula huTuMab-L- $\beta$ -Gluc, wherein huTuMab is a human tumor specific monoclonal antibody or an antigen binding fragment thereof, L is said linker molecule, and  $\beta$ -Gluc is a human  $\beta$ -glucuronidase.

34. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 22, that is synthesized in hosts selected from the group consisting of mammalian cells, microorganisms, insect cells and transgenic animals.

35. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 33, wherein said mammalian cells are Chinese Hamster Ovary (CHO) cells, and said cells are selected for a high level of expression of said glycoprotein.

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36. A bifunctional fusion glycoprotein or conjugate thereof as claimed in claim 22 in a pharmaceutically acceptable vehicle.

37. A pharmaceutical kit comprising:

(a) a first component comprising a bifunctional fusion glycoprotein or conjugate thereof comprising

(i) at least one first portion which possesses enzymatic activity; and

(ii) at least one second portion which comprises a molecular structure that binds said first component to a tumor-specific antigen on a tumor cell;

wherein said glycoprotein or conjugate thereof comprises at least one carbohydrate complement comprising at least one exposed carbohydrate residue selected from the group consisting of mannose, galactose, N-acetylglucosamine, N-acetyllactose, glucose and fucose; and

(b) a second component comprising a non-toxic prodrug that is subsequently cleaved into a tumor cytotoxic drug by said enzymatic activity of said first component,

wherein said pharmaceutical kit lacks an additional component that affects clearance of said first component and wherein each of said first and said second components is in a pharmaceutically acceptable vehicle.

38. A kit as claimed in claim 37, wherein said exposed carbohydrate residue is a galactose or a mannose.

39. A kit as claimed in claim 37, wherein said exposed carbohydrate residue is a lactose.

40. A kit as claimed in claim 37, wherein said exposed carbohydrate residue is produced by enzymatic degradation of the carbohydrate complement of said glycoprotein.

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41. A kit as claimed in claim 40, wherein said enzymatic degradation is effected by an enzyme selected from the group consisting of endoglycosidases, exoglycosidases, neuraminidases and a combination thereof.

42. A kit as claimed in claim 37, wherein said exposed terminal carbohydrate residue is produced by chemical degradation of the carbohydrate complement of said glycoprotein.

43. A kit as claimed in claim 37, wherein said exposed terminal carbohydrate residue is added to said compound by chemical means.

44. A kit as claimed in claim 37, wherein said first portion consists essentially of an enzyme.

45. A kit as claimed in claim 44, wherein said enzyme is selected from the group consisting of penicillin G amidase, penicillin V amidase,  $\beta$ -lactamase, alkaline phosphatase, carboxypeptidase G2, carboxypeptidase A, cytosine deaminase, nitroreductase, diaphorase, arylsulfatase, glycosidase,  $\beta$ -glucosidase, and  $\beta$ -glucuronidase.

46. A kit as claimed in claim 37, wherein said first portion is a catalytic antibody.

47. A kit as claimed in claim 37, wherein said tumor specific antigen to which said second portions binds comprises a tumor associated antigen selected from the group consisting of CEA, N-CAM, N-cadherin, PEM, GICA, TAG-72, TF $\beta$ , GM3, GD3, GM2, GD2, GT3, HMWMAA, pMe117, gp113 (Muc18), p53, p97, MAGE-1, gp105, erbB2, EGF-R, PSA, transferrin-R, P-glycoprotein and cytokeratin.

48. A kit as claimed in claim 37, wherein said second portion consists essentially of an antibody or an antigen binding fragment thereof.

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49. A kit as claimed in claim 48, wherein said antibody or said antigen binding fragment thereof is a humanized antibody.

50. A kit as claimed in claim 49, wherein said antibody is a monoclonal antibody or an antigen binding fragment thereof.

51. A kit as claimed in claim 50, wherein said monoclonal antibody is the monoclonal antibody BW 431/26 or an antigen binding fragment thereof.

52. A kit as claimed in claim 37, wherein said first portion and said second portion are connected by a linker molecule.

53. A kit as claimed in claim 52, wherein said first component comprises the formula huTuMab-L- $\beta$ -Gluc, wherein huTuMab is a human tumor specific monoclonal antibody or an antigen binding fragment thereof, L is said linker molecule, and  $\beta$ -Gluc is a human  $\beta$ -glucuronidase.

54. A kit as claimed in claim 37, wherein said glycoprotein or conjugate thereof is synthesized in hosts selected from the group consisting of mammalian cells, microorganisms, insect cells and transgenic animals.

55. A kit as claimed in claim 54, wherein said mammalian cells are Chinese Hamster Ovary (CHO) cells, and said cells are selected for a high level of expression of said glycoprotein.

56. A kit as claimed in claim 37, further comprising an agent capable of lowering the pH in a tumor to be treated, said agent in a pharmaceutically acceptable vehicle.

57. A kit as claimed in claim 37, further comprising galactose in a pharmaceutically acceptable vehicle.

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58. A method of treating a tumor in a subject, comprising:

(a) administering to said subject in a first step, a first component

comprising a bifunctional fusion glycoprotein or conjugate thereof comprising

(i) at least one first portion which possesses enzymatic activity; and

(ii) at least one second portion which comprises a molecular structure that binds said first component to a tumor-specific antigen on a tumor cell;

wherein said glycoprotein or conjugate thereof comprises at least one carbohydrate complement comprising at least one exposed carbohydrate residue selected from the group consisting of mannose, galactose, N-acetylglucosamine, N-acetyllactose, glucose and fucose; and

(b) administering to said subject in a second step, a second component comprising a non-toxic prodrug that is subsequently cleaved into a tumor cytotoxic drug by said enzymatic activity of said first component,

wherein said method excludes the administration of an additional component that affects clearance of said first component and wherein each of said first and said second components is in a pharmaceutically acceptable vehicle.

59. A process of making a bifunctional fusion glycoprotein or conjugate thereof comprising the steps of:

a) preparing a DNA encoding a fusion glycoprotein or conjugate thereof according to claim 22;

b) inserting said DNA in an expression vector;

c) expressing said DNA in a eukaryote expression system so as to produce said fusion glycoprotein or conjugate thereof; and,

d) isolating said expressed fusion glycoprotein or conjugate thereof.

60. A process according to claim 59, wherein said eukaryote expression system is selected from the group consisting of mammalian cells, microorganisms, insect cells and transgenic non-human mammals.

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61. A process according to claim 60, wherein said mammalian cells are Chinese Hamster Ovary (CHO) cells, and said cells are selected for a high level of expression of said glycoprotein.

62. A process as claimed in claim 59, wherein said exposed carbohydrate residue is produced by enzymatic degradation of the carbohydrate complement of said glycoprotein.

63. A process as claimed in claim 62, wherein said enzymatic degradation is effected by an enzyme selected from the group consisting of endoglycosidases, exoglycosidases, neuraminidases and a combination thereof.

64. A process as claimed in claim 59, wherein said exposed terminal carbohydrate residue is produced by chemical degradation of the carbohydrate complement of said glycoprotein.

65. A process as claimed in claim 59, wherein said exposed terminal carbohydrate residue is added to said compound by chemical means.--

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